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学位論文の題名	<p>Clinical impact of the presence of macrophages in endomyocardial biopsies of patients with dilated cardiomyopathy (拡張型心筋症患者における心筋生検検体内にみられるマクロファージ出現の臨床的意義)</p> <p>European Journal of Heart Failure 2017 Apr;19(4):490-498.</p>
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## **ABSTRACT**

### **BACKGROUND**

Dilated cardiomyopathy (DCM) is the most common cardiomyopathy and causes left ventricular enlargement and contractile dysfunction, with a poor prognosis. The mechanisms underlying the disease process have not been precisely identified, but recent evidence has suggested that the activation of myocardial inflammation is involved in the deterioration associated with the condition.

### **METHODS**

Biopsy samples from 182 consecutive DCM patients were immunohistochemically stained with antibodies specific to CD3 (T lymphocytes), CD68 (whole macrophages) and CD163 (M2 macrophages), and each type of infiltrating cell was counted. Masson's trichrome staining was used to measure the collagen area fraction (CAF) in each sample. Patients were followed up for  $6.9 \pm 2.4$  years, and their clinical data were obtained for analysis.

### **RESULTS**

Median (interquartile) numbers of myocardial CD3, CD68 and CD163-cell infiltrates were 8.1 (4.0–14.2)/mm<sup>2</sup>, 22.3 (12.1–36.0)/mm<sup>2</sup>, 6.5 (2.0–14.0)/mm<sup>2</sup>, respectively. Patients with higher counts of infiltrating CD3<sup>+</sup>, CD68<sup>+</sup> and CD163<sup>+</sup>-positive cells had significantly poorer outcomes ( $p = 0.007$ ,  $p = 0.011$  and  $p = 0.022$ , respectively). A high CD163-positive infiltrate count was independently associated with worse outcome in multivariate Cox regression analysis (hazard ratio = 1.77,  $p = 0.004$ ), and multivariate linear regression analysis revealed that the CD163 cell count was an independent determinant of CAF ( $p < 0.001$ ).

### **CONCLUSIONS**

DCM with increased myocardial immune activation was associated with poor long-term outcome. The relationship between M2 macrophages and collagen formation suggests the phenotypic polarisation of macrophages toward M2 may be associated with ventricular remodeling in DCM.